10/086,913

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=> d his

     (FILE 'HOME' ENTERED AT 16:52:27 ON 21 FEB 2006)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 16:52:54 ON 21 FEB 2006
L1          1043 S (ONCOGENEIS OR CANCER OR CELL (A) PROLIFERAT?) AND MYCOPLASMA
L2        115017 S (SIALIC (W) ACID?) OR TRANS-SIALIDASE? OR NEURAMINIDASE?
L3            24 S L1 AND L2
L4            13 DUP REM L3 (11 DUPLICATES REMOVED)
                 E HIGUCHI  M/AU
                 E HIGUCHI  M D L/AU
                 E SCHENKMAN S/AU
L5           357 S E3
L6           489 S E3-E8
L7           241 S L2 AND L6
L8             3 S L1 AND L7
L9             3 DUP REM L8 (0 DUPLICATES REMOVED)

=>
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=> file medline embase biosis biotechds scisearch hcaplus ntis lifesci
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FILE 'LIFESCI' ENTERED AT 16:52:54 ON 21 FEB 2006
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=> s (oncogeneis or cancer or cell (a) proliferat?) and mycoplasma
   6 FILES SEARCHED...
L1         1043 (ONCOGENEIS OR CANCER OR CELL (A) PROLIFERAT?) AND MYCOPLASMA

=> s (sialic (w) acid?) or trans-sialidase? or neuraminidase?
L2       115017 (SIALIC (W) ACID?) OR TRANS-SIALIDASE? OR NEURAMINIDASE?

=> s l1 and l2
L3           24 L1 AND L2

=> dup rem l3
PROCESSING COMPLETED FOR L3
L4            13 DUP REM L3 (11 DUPLICATES REMOVED)

=> d 1-13 ibib ab

L4    ANSWER 1 OF 13  BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
      DUPLICATE 1
ACCESSION NUMBER: 2005-23036  BIOTECHDS
TITLE:            Immune response altering agent useful for treating autoimmune
                  diseases, comprises first domain having T/B cell epitopes or
                  Toll-like receptor-binding proteins, and second domain having
                  heterologous target molecule;
                     vector-mediated gene transfer and expression in host cell
                     for recombinant T-lymphocyte, B-lymphocyte epitope
                     production for use in disease therapy
AUTHOR:           MAHAIRAS G G
PATENT ASSIGNEE:  VIEVAX CORP
PATENT INFO:      WO 2005070959 4 Aug 2005
APPLICATION INFO: WO 2005-US2251 24 Jan 2005
PRIORITY INFO:    US 2004-616855 6 Oct 2004; US 2004-538713 23 Jan 2004
DOCUMENT TYPE:    Patent
LANGUAGE:         English
```

OTHER SOURCE: WPI: 2005-542270 [55]

AB DERWENT ABSTRACT:

NOVELTY - An immune response altering agent (I) comprises a first domain having one or more components chosen from T cell epitopes, B cell epitopes, and Toll-like receptor (TLR)-binding proteins or its TLR-binding domains, and a second domain having heterologous target molecule against which an immune response is desired, where the first domain alters an immune response in a subject against the heterologous target.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for: (1) a composition (C1) comprising (I) in combination with an excipient or an adjuvant; (2) a T cell epitope cassette (II) comprising multiple T cell epitopes, where (II) alters an immune response to a heterologous target when administered as a fusion with, or attached to the heterologous target; (3) a composition (C2) comprising a heterologous target molecule, and one or more first domains, where the first domains comprise a polypeptide sequence chosen from either one of the full length polypeptide sequences having a fully defined 95 and 100 amino acid (SEQ ID Number 214 and 215) sequences given in the specification (early secretory antigenic target 6 (ESAT6) and culture filtrate protein 10 (CFP10)), and their fragment that induces an immune response that is not substantially reduced as compared to immune response induced by the full length polypeptide; and (4) inducing or enhancing (M1) an immune response to a target molecule in an individual, involves administering a composition comprising the target molecule and one or more polypeptides or their fragments, where one or more polypeptides or their fragments comprise one or more T cell epitopes.

BIOTECHNOLOGY - Preferred Agent: In (I), the T cell epitopes are derived from more than one source, where the source comprises an infectious agent, preferably virus, bacteria, fungus, yeast or **mycoplasma**. The source comprises a tumor, tumor antigen, autoantigen, non-self antigen or self-antigen. The first domain is covalently attached to the second domain through a peptide bond, chemically coupled to the second domain, non-covalently attached to the second domain, mechanically attached to the second domain, or enzymatically attached to the second domain. The first domain is attached to the second domain through an electrostatic interaction or hydrophobic interaction. The first domain is attached to the second domain through biotin or an antibody. The heterologous target comprises a protein, non-proteinaceous molecule, polysaccharide, glycolipid, lipopolysaccharide, tumor antigen, autoantigen, cytomegalovirus (CMV) protein, respiratory syncytial virus (RSV) protein, Streptococcus pneumoniae protein, Chlamydia protein, hepatitis C protein, herpes virus protein, measles protein or influenza protein. The T cell epitopes are generated synthetically or recombinantly. The T cell epitopes comprise CD4+ T helper cell epitopes and/or CD8+ cytotoxic T cell epitopes. (I) is a polynucleotide encoding a fusion protein, or a fusion protein. Preferred Composition: In (C2), the polypeptide comprises SEQ ID Number 214 and/or 215. The fragment consists of at least 9 or 20 contiguous residues. The first domain comprises a polypeptide comprising one of 77 fully defined 10-20 amino acid sequences (SEQ ID Number 216-293) given in the specification. Preferred Method: In (M1), the target molecule is a non-protein antigen, where the non-protein antigen is chosen from bacterial polysaccharide, glycolipid, lipopolysaccharide and a lipoprotein. The agent is attached to a targeting molecule, where the targeting molecule is an antibody or its antigen-binding fragment.

ACTIVITY - Antibacterial; Virucide; Fungicide; Anti-HIV; Hepatotropic; Antiparasitic; Cytostatic; Immunosuppressive; Antiarthritic; Antirheumatic; Neuroprotective; Antidiabetic; Gastrointestinal-Gen.; Antiinflammatory; Antiulcer; Antipsoriatic; Dermatological; Antiasthmatic; Antiallergic. No supporting data is given.

MECHANISM OF ACTION - Immunomodulator (claimed).

USE - (I) is useful for altering or inducing an immune response to a target, which involves administering (I) to a subject, where the target

is an autoantigen, tumor antigen or an antigen derived from an infectious agent. The immune response is altered from a Th2 type response to a Th1 type response. The immune response includes CD8 cytotoxic T cell mediated response or CD4 T helper cell mediated response. The immune response is predominantly Th1 or Th2 type response. (C2) is useful for inducing or enhancing an immune response to a heterologous target molecule in an individual, which involves administering C2 to a subject. The immune response is Th0 type response, CD4+ T cell response, or CD8+ T cell response. The target molecule comprises an antigen chosen from viral coat protein, influenza, **neuraminidase**, influenza hemagglutinin, HIV glycoprotein 160 or their derivatives, severe acute respiratory syndrome (SARS) coat protein, herpes virion proteins, West Nile virus (WNV) capsid proteins, pneumococcal surface adhesion A (PsaA), pneumococcal surface protein A (PspA), N-acetylmuramoyl-L-alanine amidase (LytA), Neisseria gonorrhoeae outer membrane protein (OMP) or N.gonorrhoeae surface proteases (all claimed). (I) or (C1) is also useful for treating viral infections (e.g., HIV and hepatitis C virus), bacterial infections (e.g., Staphylococcus and Pseudomonas), parasites (e.g., Leishmania), fungal infections (e.g., Candida), **cancer** (e.g., non-Hodgkin's lymphoma, Hodgkin's disease and leukemia), and autoimmune diseases such as rheumatoid arthritis, multiple sclerosis, insulin dependent diabetes, Addison's disease, celiac disease, inflammatory bowel disease, ulcerative colitis, Crohn's disease, systemic lupus erythematosus, psoriasis, Sjogren's syndrome, etc. (I), (C1) or (C2) is useful for treating inflammatory and hyperproliferative skin diseases, and allergic reactions such as asthma, bronchitis, allergic rhinitis etc.

ADMINISTRATION - (C1) is administered by intravenous, subcutaneous, intramuscular, intraperitoneal, intrarectal, intravaginal, intranasal, intragastrical, intratracheal, intrapulmonary or oral route. No specific dosage is given.

ADVANTAGE - (I) alters an immune response generated against the heterologous target molecule. (I) can be applied to wide range of species such as humans, non-human primates, horses, etc.

EXAMPLE - No relevant example is given.(130 pages)

L4 ANSWER 2 OF 13 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
DUPLICATE 2

ACCESSION NUMBER: 2005-21502 BIOTECHDS

TITLE: New nucleic acid comprising Listeria monocytogenes hly 5' UTR or actA 5' UTR, a ribosome binding site (RBS) and a heterologous nucleic acid sequence, useful in inducing an immune response to a bacterial, fungal, parasitic or **cancer** antigen;
bacterium protein production and expression vector for use in vaccine and gene therapy

AUTHOR: HIGGINS D E; SHEN A

PATENT ASSIGNEE: HIGGINS D E; SHEN A

PATENT INFO: US 2005147621 7 Jul 2005

APPLICATION INFO: US 2004-961291 8 Oct 2004

PRIORITY INFO: US 2004-961291 8 Oct 2004; US 2003-510599 10 Oct 2003

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: WPI: 2005-487940 [49]

AB DERWENT ABSTRACT:

NOVELTY - An isolated nucleic acid (I) comprising a 5' untranslated region (UTR) from Listeria monocytogenes, a ribosome binding site, and a heterologous nucleic acid operably linked to the UTR, is new.

DETAILED DESCRIPTION - An isolated nucleic acid (I) comprises: (a) a 5' untranslated region (UTR) chosen from a Listeria monocytogenes hly 5' and actA 5' UTRs, and their functional fragments and variants; (b) a ribosome binding site (RBS); and (c) a heterologous nucleic acid sequence operably linked to the 5' UTR. INDEPENDENT CLAIMS are also included for: (1) an isolated nucleic acid comprising a L. monocytogenes 5' UTR chosen from an hly 5' UTR and an actA 5' UTR; (2) a nucleic acid vector

comprising: (a) a Listeria monocytogenes promoter; (b) a Listeria monocytogenes hly or actA 5' UTR comprising a ribosome binding site; (c) a heterologous nucleic acid sequence; (d) a selectable marker; and (e) a bacterial origin of replication, where the UTR is operably linked to the promoter and the heterologous nucleic acid sequence; (3) a bacterium comprising a nucleic acid comprising the same components as the vector of (2); (4) a vaccine comprising the bacterium; (5) a vaccine comprising the isolated nucleic acid (I); (6) introducing an antigen into a eukaryotic cell comprising contacting the cell with the bacterium of (3); (7) inducing an immune response to an antigen in a subject by administering bacteria of (3); and (8) expressing a polypeptide by introducing nucleic acid (I) into a bacterium, where the heterologous nucleic acid encodes a polypeptide, and expressing the polypeptide.

BIOTECHNOLOGY - Preferred Nucleic Acid: The nucleic acid (I) further comprises a promoter and preferably also a transcriptional activation site 5' of the promoter. The transcriptional activation site is a prfA box. The ribosome binding site (RBS) is the RBS that is naturally associated with the L. monocytogenes UTR. The hly 5' UTR comprises a nucleotide sequence at least 70% homologous to the sequence AGAGAGGGGTGGCAAACGGTATTTGGCATTATTAGGTTTGTAGAAGGAGAGTGAAACCC (SEQ ID NO. 3). The hyl 5' UTR comprises a nucleotide sequence at least 70% homologous to the sequence AGAAGCGAATTTCGCCAATATTATAATTATCAAAAGAGAGGGGTGG CAAACGGTATTTGGCATTATTAGGTTAAAAAATGTAGAAGGAGAGTGAAACCC (SEQ ID NO: 2). The hly 5' UTR comprises a nucleotide sequence at least 70% homologous to the sequence ATAAAGCAAGCATATAATATTGCGTTTCATCTTTAGAAGCGAATTTCGCCAATATTATAATTAT CAAAAGAGAGGGGTGGCAACGGTATTTGGCATTATTAGGTTAAAAAATGTAGAAGGAGAGTGAAACC (SEQ ID NO: 1). The actA 5' UTR comprises a nucleotide sequence at least 70% homologous to the sequence GTGAAAATGAAGGCCGAATTTTCCTTGTTCTAAAAAGGTTGTATTA GCGTATCACGAGGAGGGAGTATAA (SEQ ID NO. 7). The actA 5' UTR comprises a nucleotide sequence at least 70% homologous to the sequence GCTAATCCAATTTTTAACGGAATAAATTAGTGAAAATGAAGGCCGAATTTTCCTTGTTCTAAAAAGGTTGTAT TAGCGTATCACGAGGAGGGAGTATAA (SEQ ID NO. 6). The actA 5' UTR comprises a nucleotide sequence at least 70% homologous to the sequence TAATTCATGAATATTTTTTCTTATATTAGCTAATTAAGAAGATAATTAACTGCTAATCCAATTTTTAACGGAA TAAATTAGTGAAAATGAAGGCCGAATTTTCCTTGTTCTAAAAAGGTTGTATTAGCGTATCACGAGGAGGGAGT ATAA (SEQ ID NO: 5). The nucleic acid comprises an integration site. The heterologous nucleic acid encodes a viral polypeptide or its antigenic fragment. The heterologous nucleic acid encodes an inhibitory RNA or its portion. The viral polypeptide is a viral polypeptide encoded by human immunodeficiency virus, hepatitis B virus, hepatitis C virus, hepatitis A virus, smallpox, influenza viruses, human papilloma viruses, adenoviruses, rhinoviruses, coronaviruses, herpes simplex virus, respiratory syncytial viruses, rabies or coxsackie virus. The viral polypeptide comprises influenza antigens such as hemagglutinin (HA), nucleoprotein (NP), matrix protein (MP1); HIV antigens such as HIV gag, pol, env, tat, reverse transcriptase hepatitis; viral antigens such as the S. M, and L proteins of hepatitis B virus, the pre-S antigen of hepatitis B virus, and other hepatitis, e.g., hepatitis A, B, and C, viral components such rubella virus components; rotaviral antigens such as VP7sc and other rotaviral components; cytomegaloviral antigens such as envelope glycoprotein B and other cytomegaloviral antigen components; respiratory syncytial viral antigens such as the RSV fusion protein, the M2 protein and other respiratory syncytial viral antigen components; herpes simplex viral antigens such as immediate early proteins, glycoprotein D, and other herpes simplex viral antigen components; varicella zoster viral antigens such as gpI, gpII, and other varicella zoster viral antigen components; Japanese encephalitis viral antigens such as proteins E, M-E, M-E-NS 1, NS 1, NS 1-NS2A, and other Japanese encephalitis viral antigen components; rabies viral antigens such as rabies glycoprotein, rabies nucleoprotein and other rabies viral antigen components; and Hepatitis B surface antigen; hepatitis C viral RNA; influenza viral antigens such as hemagglutinin and **neuraminidase** and other influenza viral components; measles viral antigens such as the measles virus fusion protein and other measles virus components; rubella

viral antigens such as proteins E1 and E2. The heterologous nucleic acid sequence encodes a mammalian polypeptide. The mammalian polypeptide is a **cancer**-associated polypeptide or its antigenic fragment. The nucleic acid **cancer**-associated polypeptide comprises 707 alanine proline (707-AP); alpha ((x)-fetoprotein (AFP); adenocarcinoma antigen recognized by T cells 4 (ART-4); B antigen (BAGE); beta-catenin/mutated(b-catenin/m); breakpoint cluster region-Abelson (Bcr-abl); CTL-recognized antigen on melanoma (CAMEL); carcinoembryonic antigen peptide-1 (CAP-1); caspase-8 (CASP-8); cell-division cycle 27 mutated (CDC27m); cyclin-dependent kinase 4 mutated CDK4/m); carcinoembryonic antigen (CEA); **cancer**/testis (CT) antigen; cyclophilin B (Cyp-B); differentiation antigen melanoma (DAM-6, also known as MAGEB2, and DAM-10, also known as MAGE-B1); elongation factor 2 mutated (ELF2M); Ets variant gene 6/acute myeloid leukemia i gene ETS (ETV6-AML1); glycoprotein 250 (G250); G antigen (GAGE); N-acetylglucosaminyltransferase V (GnT-V); glycoprotein 100 kD (GnT-V); helicase antigen (HAGE); human epidermal receptor-2/neurological (HER-2/neu); HLA-Aasterisk0201-R1701 (HLA-Aasterisk0201 having an arginine (R) to isoleucine (I) exchange at residue 170 of the (x-helix of the (x2-domain in the HLA-A2 gene); human papilloma virus E7 (HPV-E7); human papilloma virus E6 (HPV-E6); heat shock protein 70-2 mutated (HSP70-2M); human signet ring tumor-2 (HST-2); human telomerase reverse transcriptase (hTERT or hTRT); intestinal carboxyl esterase (iCE); KIAA0205; L antigen (LAGE); low density lipid receptor/GDP-L-fucose: beta-D-galactosidase 2-(alpha-Lfucosyltransferase (LDLR/FUT); melanoma antigen (MAGE); melanoma antigen recognized by T cells-1/Melanoma antigen A (MART-1/Melan-A); melanocortin i receptor (MCiR); myosin mutated (myosin/m); mucin 1 (MUC 1); melanoma ubiquitous mutated 1 (MUM-1), melanoma ubiquitous mutated 2 (MUM-2), melanoma ubiquitous mutated 3 (MUM-3); New York-esophageous 1 (NY-ESO-1); protein 15 (P15); protein of 190 KD bcr-abl (p190 minor bcr-abl); promyelocytic leukemia/retinoic acid receptor alpha (Pml/ RARa); preferentially expressed antigen of melanoma (PRAME); prostate-specific antigen (PSA); prostate-specific membrane antigen (PSM); renal antigen (RAGE); renal ubiquitous i (RU1), renal ubiquitous 2 (RU2); sarcoma antigen (SAGE); SART-1; SART-3; translocation Ets-family leukemia/acute myeloid leukemia 1 (TEL/AML1); triosephosphate isomerase mutated (TPI/m); tyrosinase related protein i (TRP-1 or gp75); tyrosinase related protein 2 (TRP2); TRP-2/intron 2 (TRP-2/INT2); Wilms' tumor gene (WT-1). The heterologous nucleic acid sequence encodes a bacterial polypeptide or its antigenic fragment. The nucleic acid bacterial polypeptide is a bacterial polypeptide encoded by one of the following bacteria: Mycobacterium spp. (e.g., Mycobacterium tuberculosis, Mycobacterium leprae), Streptococcus spp. (e.g., Streptococcus pneumoniae, Streptococcus pyogenes), Staphylococcus spp. (e.g., Staphylococcus aureus), Treponema (e.g., Treponema pallidum), Chlamydia spp., Vibrio spp. (e.g., Vibrio cholerae), Bacillus spp. (e.g., Bacillus subtilis Bacillus anthracis), Yersinia spp. (e.g., Yersinia pestis), Neisseria spp. (e.g., Neisseria meningitides, Neisseria gonorrhoeae), Legionella spp., Bordetella spp. (e.g., Bordetella pertussis), Shigella spp., Campylobacter spp., Pseudomonas spp. (e.g., Pseudomonas aeruginosa), Brucella spp., Clostridium spp. (e.g., Clostridium tetani, Clostridium botulinum, Clostridium perfringens), Salmonella spp. (e.g., Salmonella typhi), Borrelia spp. (e.g., Borrelia burgdorferi), Rickettsia spp. (e.g., Rickettsia prowazeki), **Mycoplasma** spp. (e.g., **Mycoplasma** pneumoniae), Haemophilus spp. (e.g., Haemophilus influenzae), Branhamella spp. (e.g., Branhamella catarrhalis), Corynebacteria spp. (e.g., Corynebacteria diphtheriae), Klebsiella spp. (e.g., Klebsiella pneumoniae), Escherichia spp. (e.g., Escherichia coli), and Listeria spp. (e.g., Listeria monocytogenes). The bacterial polypeptide comprises listeriolysin O, L. monocytogenes p60, L. monocytogenes metalloprotease (MPL), Chlamydia Capl, Chlamydia Cap2, M. tuberculosis heat shock protein (hsp)60, M. tuberculosis hsp70, M. tuberculosis Ag85, M. tuberculosis' ESAT-6 and M. tuberculosis' CFP10. The heterologous nucleic acid sequence encodes a parasitic or fungal

polypeptide. The parasitic or fungal polypeptide is a polypeptide encoded by one of the following parasites or fungi: Candida spp. (e.g., Candida albicans), Cryptococcus spp. (e.g., Cryptococcus neoformans), Aspergillus spp., Histoplasma spp. (e.g., Histoplasma capsulatum), Coccidioides spp. (e.g., Coccidioides immitis), Pneumocystis (e.g., Pneumocystis carinio, Entamoeba spp. (e.g., Entamoeba histolytica), Giardia spp., Leishmania spp., Plasmodium spp., Trypanosoma spp., Toxoplasma spp. (e.g., Toxoplasma gondii), Cryptosporidium spp., Trichuris spp. (e.g., Trichuris trichiura), Trichinella spp. (e.g., Trichinella spiralis), Enterobius spp. (e.g., Enterobius vermicularis), Ascaris spp. (e.g., Ascaris lumbricoides), Ancylostoma spp., Strongyloides spp., Filaria spp., and Schistosoma spp. The parasitic polypeptide is MSP-1; malarial antigens 41-3, AMA-1, CSP, PFEMP-1, GBP-130, MSP-1, PFS-16, SERP; fungal antigens such as heat shock protein 60; plasmodium falciparum antigens such as merozoite surface antigens, sporozoite surface antigens, circumsporozoite antigens, gametocyte/gamete surface antigens, blood-stage antigen pf i 55/RESA and other plasmodial antigen components; toxoplasma antigens such as SAG-1, p30 and other toxoplasma antigen components; schistosomae antigens such as glutathione-S-transferase, paramyosin, and other schistosomal antigen components; leishmania major and other leishmaniae antigens such as gp63, lipophosphoglycan and its associated protein and other leishmanial antigen components; and Trypanosoma cruzi antigens such as the 75-77 kDa antigen, the 56 kDa antigen and other trypanosomal antigen components. The Listeria monocytogenes 5' UTR increases expression of a polypeptide encoded by the heterologous nucleic acid sequence at least 1.5-fold, 2-fold, 5-fold, 10-fold, 30-fold, or 50-fold relative to a polypeptide encoded by the heterologous nucleic acid sequence that is not operably linked to the UTR. Preferred Bacterium: The bacterium is a Listeria monocytogenes bacterium, a Bacillus subtilis bacterium or a Lactococcus lactis bacterium.

ACTIVITY - Antiviral; Antibacterial; Fungicide; Antiparasitic; Cytostatic. No biological data given.

MECHANISM OF ACTION - Vaccine; Gene therapy.

USE - The nucleic acid and the bacterium containing the nucleic acid are useful as antiviral, antibacterial, antifungal, antiparasitic and **cancer** vaccines. The nucleic acid is useful for expressing an inhibitory RNA. A bacterium transfected by the nucleic acid is useful for production of a polypeptide. (All claimed).

ADVANTAGE - The hly and actA 5' UTRs give enhanced expression of heterologous nucleic acids. Bacteria (e.g. Listeria monocytogenes, Bacillus subtilis or Lactococcus lactis) transfected with a nucleic acid including one of the 5' UTRs may be used for expression of a heterologous polypeptide, especially where expression in a bacterium such as Escherichia coli is not appropriate, e.g. where the polypeptide is toxic to E. coli.(26 pages)

L4 ANSWER 3 OF 13 MEDLINE on STN DUPLICATE 3

ACCESSION NUMBER: 2005364047 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16020660
TITLE: p37 Induces tumor invasiveness.
AUTHOR: Ketcham Catherine M; Anai Satoshi; Reutzel Robbie; Sheng Shijie; Schuster Sheldon M; Brenes Ryan B; Agbandje-McKenna Mavis; McKenna Robert; Rosser Charles J; Boehlein Susan K
CORPORATE SOURCE: Department of Biochemistry and Molecular Biology, College of Medicine, University of Florida, Gainesville, 32610, USA.
CONTRACT NUMBER: CA84176 (NCI)
SOURCE: Molecular cancer therapeutics, (2005 Jul) 4 (7) 1031-8. Journal code: 101132535. ISSN: 1535-7163.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200512

ENTRY DATE: Entered STN: 20050716
Last Updated on STN: 20051224
Entered Medline: 20051223

AB Previous studies have shown a statistically significant correlation between human carcinomas and monoclonal antibody detection of a **Mycoplasma** hyorhinis-encoded protein known as p37. A potential mechanism of p37 is that it might promote invasion and metastasis. Recombinant p37 enhanced the invasiveness of two prostate carcinoma and two melanoma cell lines in a dose-dependent manner in vitro, but did not have a significant effect on tumor cell growth. Furthermore, the increased binding to cell surfaces and the enhanced invasive potential of **cancer** cells from exposure to p37 could be completely reversed by preincubation of the **cancer** cells with an anti-p37 monoclonal antibody. Sequence comparisons, followed by three-dimensional molecular modeling, revealed a region of similarity between p37 and influenza hemagglutinin A, a **sialic acid**-binding protein that plays a critical role in viral entry. Binding of p37 to prostate carcinoma cells was found to be at least partially **sialic acid** dependent because **neuraminidase** treatment decreased this binding. Taken together, these observations suggest that M. hyorhinis can infect humans and may facilitate tumor invasiveness via p37. These results further suggest that p37 may be a molecular target for **cancer** therapy.

L4 ANSWER 4 OF 13 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2004419768 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15325005
TITLE: Trypanosoma cruzi **trans-sialidase** as a new therapeutic tool in the treatment of chronic inflammatory diseases: possible action against **mycoplasma** and chlamydia.
AUTHOR: de Lourdes Higuchi Maria
CORPORATE SOURCE: Pathology Laboratory, Heart Institute (InCor) of Clinical Hospital, School of Medicine of Sao Paulo University, Av. Dr Eneas de Carvalho Aguiar 44, 05403-000 Sao Paulo, SP, Brazil.. anplourdes@incor.usp.br
SOURCE: Medical hypotheses, (2004) 63 (4) 616-23.
Journal code: 7505668. ISSN: 0306-9877.
PUB. COUNTRY: Scotland: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200502
ENTRY DATE: Entered STN: 20040825
Last Updated on STN: 20050216
Entered Medline: 20050215

AB The present paper proposes a new therapy using Trypanosoma cruzi **trans-sialidase** to treat diseases with unclear pathogenesis that present in common chronic inflammation and fibrosis. This hypothesis is based on recent findings that co-infection with **mycoplasma** and chlamydia is present in many of these diseases and that this enzyme was capable to eliminate or decrease the co-infection from the host. We identified that **mycoplasmas** and chlamydias are present in atherosclerosis, aortic valve stenosis, dilated cardiomyopathy, chronic chagasic myocarditis and **cancer**. We hypothetized that mycoplasmal infection may induce immunodepression in the host, favoring proliferation of pre-existent chlamydial infection and that elimination of **mycoplasma** would lead to improvement of the immune system resistance and the control of chlamydial proliferation. **Mycoplasma** has a particular parasitic relationship with host cells, involving strong adherence of their membranes, making it extremely difficult to eradicate mycoplasmal infection from the host. A new therapeutic approach is suggested using one or more agents that prevent or inhibit the adherence of **mycoplasma** to host cell membranes by

removing **sialic acid** residues and preventing oxidation of the cells. The use of a **neuraminidase** enzyme, particularly the T. cruzi **trans-sialidase** enzyme, associated with treatment using anti-oxidating agents is proposed. Preliminary experimental animal and laboratory tests showed good results. The proposal that **trans-sialidase** from T. cruzi is efficient in combating co-infection of **mycoplasma** and chlamydia is based, at least in part, on the observation that chagasic patients suffering from T. cruzi infection present less **mycoplasma** and chlamydia infection in their tissues. Also, a lower incidence of the diseases above described to be related to **mycoplasma** infection is observed in chagasic patients. It is also hypothesized that co-infection with **mycoplasma** and chlamydia may induce oxidation of the host cells. Anti-oxidants such as those present in plant extracts may also be used in the treatment. Other diseases such as chronic hepatitis, glomerulonephritis, Multiple Sclerosis, Alzheimer's Syndrome and idiopathic encephalitis are other examples of chronic diseases where **mycoplasma** and chlamydia might be present, as they have the characteristics of unknown etiology, persistent chronic inflammation and fibrosis.

L4 ANSWER 5 OF 13 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
DUPLICATE 5

ACCESSION NUMBER: 2003-27952 BIOTECHDS
TITLE: Composition useful for treating **mycoplasma** infection comprises an agent that prevents proliferation of **mycoplasma** or associated microbes; native or recombinant enzyme treatment for disease therapy
AUTHOR: HIGUCHI M D L
PATENT ASSIGNEE: HIGUCHI M D L
PATENT INFO: WO 2003082324 9 Oct 2003
APPLICATION INFO: WO 2003-BR49 28 Mar 2003
PRIORITY INFO: BR 2002-1010 28 Mar 2002; BR 2002-1010 28 Mar 2002
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2003-803968 [75]

AB DERWENT ABSTRACT:

NOVELTY - A composition comprises an agent (A) that prevents or inhibits the proliferation of at least one of **Mycoplasma** or microbes associated with **Mycoplasma**, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for the use of an agent (A) for the manufacture of a medicament for treating a disorder defined by increased microbes proliferation associated with inflammation, fibrosis, calcification, ossification, cellular disarray and/or fragmentation of the extra-cellular matrix of the adjacent tissue.

ACTIVITY - Antimicrobial; Antibacterial; Antiinflammatory; Nephrotropic; Hepatotropic; Endocrine-Gen.; Cytostatic; Osteopathic; Antiarthritic; Antirheumatic; Gastrointestinal-Gen.; Cerebroprotective; Neuroprotective; Antiallergic; Vasotropic; Antiulcer; Respiratory-Gen.; Antiasthmatic; Virucide; Anti-HIV; Dermatological.

MECHANISM OF ACTION - **Mycoplasma** proliferation inhibitor; **Mycoplasma**-associated microbes proliferation inhibitor; Host **cell proliferation** inhibitor; Microbial proliferation inhibitor. Two rats presenting skin ulcer and tail injury due to the co-infection of Lycoplasm and Spirochetes were treated. One received 0.5 ml/animal TSN (complete active native **trans-sialidase** of Trypanosoma cruzi), every day for 10 days, and the other received TSC (active **trans-sialidase** substance catalytic portion, produced by a recombinant bacteria containing the Plasmodium (pTSIII), ATCC with PTA - 3483) for 8 days. The mice were killed respectively with 14 and 10 days. The skin ulcers already showed initial healing after 4 days of treatment, with complete healing in 14 days, with the formation of a new coat. There was a stop in the loss of the tail and the

histological exam demonstrated regression of the lesion and severe decrease of all infectious agents.

USE - For treating or preventing **Mycoplasma** infection including disorders defined by co-infection and fusion of **Mycoplasma** and/or at least a second microbe to a host cell or a cell fragment, causing inflammation and at least one of the tissue alterations due to fibrosis, calcification, ossification, cellular disarray or fragmentation of the extra-cellular matrix of the subjacent tissue (e.g. aortic valve stenosis with calcification, idiopathic glomerulopathy, glomerulopathy with inflammation, Lyme's disease, co-infection with chlamydia, spirochete and/or archaea); and for the manufacture of a medicament for treating a disorder defined by increased microbes proliferation (e.g. calcification of the cardiac valves, glomerulonephritis, fibrosing chronic hepatopathy, baldness, and malignant neoplasia) (claimed). Also useful for the treatment of skin ulcer, osteoarthritis, inflammatory bowel disease, chronic cerebral sclerosis disease, lymphocytic chronic arteritis, non-purulent inflammatory osteoarthrtis, multiple sclerosis, lymphocytic inflammatory vascular disease, optionally granulomatous and with non-stabilized etiology (e.g. Takayasu's disease, giant cell arteritis, Wegener's granulomatosis, thromboangiitis obliterans), rheumatoid arthritis, ulcerative colitis, Whipple's disease, gastritis, inflammatory diseases of the respiratory tract of not well established etiology (e.g. adult respiratory distress syndrome, Goodpasture's syndrome, asthma, chronic fibrosing hepatopathy, emphysema; and for the treatment or prevention of disorders associated with **mycoplasma** infection, co-infection and/or fusion of **mycoplasma** with other microbes (e.g. virus such as human immunodeficiency virus, hepatitis virus, cytomegalovirus, human papillomavirus, Epstein-Barr virus; or bacteria).

ADMINISTRATION - The **trans-sialidase** enzyme is administered in a dosage of (4 mg/day) in a period of at least 2, or a culture of Trypanosoma cruzi with a mean **trans-sialidase** activity of 140 U/day is administered every other day for one week (1 - 8 weeks). The administration is intravenous, intraperitoneal, intrathecal, oral, by inhalation, subcutaneous or intramuscular.

ADVANTAGE - The composition inhibits or prevents the adhesion and/or infection of **Mycoplasma** and the microorganisms associated with them by at least 10%. The antibiotic protein such as **neuraminidase** enzyme or the **trans-sialidase** enzyme of Trypanosoma cruzi removes the **sialic acid** residues and inhibits or prevents the attachment of **Mycoplasma** to host cells.

EXAMPLE - No relevant example given.(24 pages)

L4 ANSWER 6 OF 13 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2004-00309 BIOTECHDS
TITLE: Use of an agent that prevents or inhibits **Mycoplasma** infection, for manufacturing a medicament for treating or preventing a disorder associated with increased **cell proliferation**, e.g. atherosclerotic vascular disease or malignancy;
recombinant Trypanosoma cruzi protein application in infection, tumor and vascular disease therapy
AUTHOR: HIGUCHI M D L; SCHENKMAN S
PATENT ASSIGNEE: HIGUCHI M D L; SCHENKMAN S
PATENT INFO: US 2003124109 3 Jul 2003
APPLICATION INFO: US 2002-86913 1 Mar 2002
PRIORITY INFO: BR 2001-2648 3 Jul 2001; BR 2000-2989 3 Jul 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2003-810968 [76]
AB DERWENT ABSTRACT:
NOVELTY - Use of an agent that prevents or inhibits **Mycoplasma**

infection for manufacturing a medicament for treating a disorder associated with increased **cell proliferation**.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for a composition for treating or preventing **Mycoplasma** infection in a subject suffering from a disorder associated with increased **cell proliferation** or a co-infection with **mycoplasma** and a second microbe, comprising an agent that prevents or inhibits **sialic acid**-mediated attachment of **mycoplasma** to cells of the subject.

BIOTECHNOLOGY - Preferred Composition: The agent is an antibiotic or an enzyme having an activity consisting of **neuraminidase** and/or **trans-sialidase** activity. The enzyme is derived from a Trypanosoma cruzi microorganism, where the enzyme is a native or a recombinant enzyme. The enzyme has a fully defined sequence of 669 amino acids given in the specification. A vector containing the DNA insert having a fully defined sequence of 2010 bp given in the specification produces the enzyme.

ACTIVITY - Antibacterial; Antiarteriosclerotic; Cytostatic; Anti-HIV. A 64-year-old female patient with a palpable abdominal mass and a tumoral mass in the rectum was administered 50 ml of native **trans-sialidase** (TSN) intraperitoneally on alternate days for a period of 14 days. On day 23, with **mycoplasmas** confirmed in the bone marrow, erythromycin (500 mg/day) was given for a further 20 days. Clinical improvement and normalization of blood leukocytes was seen after 2 days. Considering the important clinical improvement and reduction in abdominal mass, a second session of TSN was administered. The patient demonstrated improvement in general clinical status. Tomography detected a reduction in tumoral mass. Results showed that **trans-sialidase** is effective as a drug in the treatment of neoplasia, removing **mycoplasmas** from the neoplastic cells leading to their apoptosis.

MECHANISM OF ACTION - **Neuraminidase**; **Trans-sialidase**.

USE - The composition or the agent that prevents or inhibits **mycoplasma** infection is useful for manufacturing a medicament for treating or preventing a disorder associated with increased **cell proliferation**, e.g. atherosclerotic vascular disease or malignant disease, or a disease associated with co-infection with **mycoplasma** and a second microbe such as human immunodeficiency virus or a Chlamydia microbe (all claimed).

ADMINISTRATION - The amount of the enzyme administered is about 106-1013 units per day. Administration may be intravenous, intraperitoneal, intrathecal, oral, by inhalation, subcutaneous, or intramuscular. (32 pages)

L4 ANSWER 7 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:76631 HCAPLUS
DOCUMENT NUMBER: 138:135831
TITLE: Antibody heteropolymer complexes preparation and uses thereof
INVENTOR(S): Taylor, Ronald P.; Craig, Maria L.; Hahn, Chang S.
PATENT ASSIGNEE(S): University of Virginia Patent Foundation, USA
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003007971	A1	20030130	WO 2002-US23141	20020717
WO 2003007971	C2	20030410		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2454226	AA	20030130	CA 2002-2454226		20020717
EP 1416945	A1	20040512	EP 2002-770383		20020717
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK					
JP 2005504741	T2	20050217	JP 2003-513576		20020717
US 2005221284	A1	20051006	US 2004-484374		20041229
PRIORITY APPLN. INFO.:			US 2001-305989P	P	20010717
			WO 2002-US23141	W	20020717

AB The improved heteropolymer complex of the present invention comprises a first monoclonal antibody specific for a C3b-like receptor [complement receptor (CR1) or CD35 in primates and factor H in other mammals, e.g., dog, mouse, rat, pig, rabbit] site chemical crosslinked (covalently linked) to a second monoclonal antibody, in which the isotype of at least the second monoclonal antibody is the isotype having the highest affinity for the Fc receptor, e.g., in humans, IgG1 or IgG3. The invention also relates to methods for immune clearance of an antigen in a mammal via the C3b-like receptor comprising administering to said mammal an improved heteropolymer complex of the invention. Also presented are methods for treating or preventing viral infection or microbial infection, septic shock, or **cancer**, in a mammal comprising administering to said mammal an improved heteropolymer complex of the invention. The present invention further relates to pharmaceutical compns. for the treatment or prevention of the above diseases comprising an improved heteropolymer complex of the invention.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:654898 HCAPLUS
DOCUMENT NUMBER: 143:126750
TITLE: Prevention and treatment of diseases associated with **Mycoplasma**
INVENTOR(S): Higuchi, Maria de Lourdes; Schenkman, Sergio
PATENT ASSIGNEE(S): Brazil
SOURCE: Braz. Pedido PI, 65 pp.
CODEN: BPXXDX
DOCUMENT TYPE: Patent
LANGUAGE: Portuguese
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
BR 2001002648	A	20030708	BR 2001-2648		20010703
CA 2383850	AA	20020110	CA 2001-2383850		20010703
US 2003124109	A1	20030703	US 2002-86913		20020301
US 2005142116	A1	20050630	US 2004-952003		20040928
PRIORITY APPLN. INFO.:			BR 2000-2989	A	20000703
			BR 2001-2648	A	20010703
			WO 2001-BR83	W	20010703
			US 2002-86913	A2	20020301
			BR 2002-1010	A	20020328
			WO 2003-BR49	A2	20030328

AB The invention pertains to treatment of diseases associated with undesirable cellular proliferation, including arteriosclerotic narrowing of blood

vessels, by preventing infection by **mycoplasmas**. This is based upon the discovery that **Mycoplasma** is involved in many cases of undesirable cellular proliferation.

L4 ANSWER 9 OF 13 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2002-08674 BIOTECHDS
TITLE: Composition useful for treatment of **mycoplasma** infection and diseases associated with **cell proliferation** e.g. malignancy or with co-infection with another microbe, comprises agent inhibiting **sialic acid**-mediated attachment of **mycoplasma**;
native or recombinant enzyme treatment and vector-mediated gene transfer and expression in host cell for disease therapy or prevention
AUTHOR: HIGUCHI M D L; SCHENKMAN S
PATENT ASSIGNEE: HIGUCHI M D L; SCHENKMAN S
PATENT INFO: WO 2002002050 10 Jan 2002
APPLICATION INFO: WO 2000-BR83 3 Jul 2000
PRIORITY INFO: BR 2000-2989 3 Jul 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-154675 [20]
AB DERWENT ABSTRACT:
NOVELTY - A composition useful for treating or preventing **mycoplasma** infection in a subject suffering from a disorder characterized by increased **cell proliferation** or by co-infection with a second microbe comprising an agent that prevents or inhibits **sialic acid**-mediated attachment of **mycoplasma** to the subject's cells, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for use of an agent preventing/inhibiting **mycoplasma** infection in medicaments to treat disorders characterized by increase **cell proliferation**.

BIOTECHNOLOGY - Preferred Composition: The agent is preferably an enzyme (native or recombinant) with **neuraminidase** and/or **trans-sialidase** activity, especially derived from Trypanosoma cruzi. It preferably has fully defined sequence (I) of 669 amino acids as given in the specification. The medicament preferably includes a vector comprising DNA insert of a fully defined sequence (II) of 2010 base pairs as given in the specification, producing the preferred enzyme having sequence (I) as above.

ACTIVITY - Antiatherosclerotic; antibacterial; antiviral; anti-HIV; cytostatic; vasotropic. A laboratory rat population was determined to be infected with both **Mycoplasma** pulmonis and Chlamydia pneumoniae using standard immunohistological techniques and histological examination of various organs. Nine adult rats (approximately 285 g; seven males, two females) presenting conjunctivitis, slow movements and, in one rat severe otitis and another severe weight loss, were allocated to groups A or B. A (Control group) comprised three animals, two of which were killed without injecting any substance and one receiving an inactivated form of 'TSC' (recombinantly produced catalytic portion of Trypanosoma cruzi **trans-sialidase**) for 5 consecutive days. B comprised five animals receiving 'TNS' (complete, native Trypanosoma cruzi **trans-sialidase**) (0.5 ml/animal, every 2 days) and sacrificed after 7, 9, and 12 days, and one rat receiving active TSC (140 microgram/day, five consecutive days) and killed after 7 days. Group B rats showed a clear improvement in symptoms, becoming more agile, requiring more ether to anesthetize them and becoming more difficult to restrain. The animal with otitis showed less equilibrium loss and the animal with severe weight loss gained weight. Since the lung was the most frequently injured organ, pulmonary alterations were examined using electron microscopy, confocal laser microscopy and immunohistochemistry. Histological sections showed that treated animals presented resolving

pneumonitis after 7 d. After 9-12 days M. pulmonis were almost absent from alveoli and mean C. pneumoniae positive cell numbers in alveoli had decreased, compatible with regression of C. pneumoniae infection. Results are given in the specification.

MECHANISM OF ACTION - Inhibits **sialic acid** mediated attachment of **mycoplasma** to cells.

USE - The compositions are useful to treat diseases associated with undesirable **cell proliferation**, such as atherosclerotic vascular disease and malignancy (both claimed), by reducing or preventing **mycoplasma** infection. They also useful to treat diseases associated with infection with other infectious organisms co-occurring with **mycoplasma** (and typically increasing the virulence of both pathogens), especially human immunodeficiency virus or chlamydia species. They can be used to treat such diseases in humans or other animals, and can be administered in conjunction with conventional agents e.g. anti-platelet or chemotherapeutic agents.(63 pages)

L4 ANSWER 10 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:977677 HCAPLUS
DOCUMENT NUMBER: 138:54549
TITLE: Uses of cytokines as adjuvants in avian vaccines
INVENTOR(S): Lowenthal, John William; Boyle, David Bernard; Quere, Pascale
PATENT ASSIGNEE(S): Institut National De La Recherche Agronomique, Fr.; Commonwealth Scientific and Industrial Research Organisation
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002102404	A1	20021227	WO 2002-AU800	20020618

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-299047P P 20010618

AB The invention relates to a method of treatment or prophylaxis of avian pathogenic disease in a bird comprising administering to the bird one or more avian cytokine polypeptides sufficient to stimulate the immune response of the bird to an antigen. The avian cytokine polypeptides may be administered directly or via a nucleic acid mol. The method may further comprise administration of an antigen administered directly or via a nucleic acid mol. The invention also includes vaccines and gene constructs for carrying out the method. The vaccines and cytokines can be used to protect birds against viral and bacterial infection and **cancer**. The cytokines are selected from colony-stimulating factor, interferon, and interleukin. The birds can be poultry, domestic, or game birds.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:597831 HCAPLUS
DOCUMENT NUMBER: 135:166024
TITLE: Methods for the prevention and treatment of infections and **cancer** using anti-C3b(i) antibodies
INVENTOR(S): Taylor, Ronald P.; Lindorfer, Margaret A.; Sutherland, William M.; Goldberg, Joanna B.
PATENT ASSIGNEE(S): The University of Virginia Patent Foundation, USA
SOURCE: PCT Int. Appl., 94 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2001058483	A2	20010816	WO 2001-US4020		20010208
WO 2001058483	A3	20020418			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
CA 2400488	AA	20010816	CA 2001-2400488		20010208
EP 1257583	A2	20021120	EP 2001-907104		20010208
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2003522159	T2	20030722	JP 2001-557591		20010208
PRIORITY APPLN. INFO.:			US 2000-181143P	P	20000208
			US 2000-724621	A	20001128
			WO 2001-US4020	W	20010208

AB The present invention relates to the treatment and prevention of viral infections, microbial infections, and septic shock by the administration of anti-C3b(i) antibodies. The present invention also relates to methods of treating and preventing viral infection, microbial infection, or septic shock in an animal comprising administering to said animal IgG antibodies, IgM antibodies and/or complement components in combination with antibodies immunospecific for C3b(i). The present invention also relates methods of treating and preventing viral infection or microbial infection in an animal comprising administering said animal antibodies that immunospecifically bind to one or more viral antigens or microbial antigens, resp., in combination with antibodies immunospecific for C3b(i). The present invention further relates methods of treating and preventing septic shock in an animal comprising administering said animal antibodies that immunospecifically bind to lipopolysaccharide, an endotoxin or a constituent of the outer wall of a gram neg. bacteria in combination with antibodies immunospecific for C3b(i). The examples discuss the use of anti-C3b(i) antibodies for the treatment and prevention of **cancer**
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L4 ANSWER 12 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:659405 HCAPLUS
DOCUMENT NUMBER: 131:285411
TITLE: Avian IL-15 nucleotides and polypeptides, and methods of immunizing poultry using avian IL-15
INVENTOR(S): Choi, Kang; Tsusaki, Yoshinari; Kamogawa, Koichi; Lillehoj, Hyun S.
PATENT ASSIGNEE(S): Nippon Zeon Co., Ltd., Japan; United States Dept. of Agriculture
SOURCE: PCT Int. Appl., 66 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9951622	A1	19991014	WO 1999-US7485	19990406
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9934720	A1	19991025	AU 1999-34720	19990406
JP 11346786	A2	19991221	JP 1999-98329	19990406
PRIORITY APPLN. INFO.:			US 1998-55293 A	19980406
			WO 1999-US7485 W	19990406

AB The present invention relates to an isolated avian IL-15 polypeptide comprising: (a) the amino acid sequence of SEQ ID NO:1; (b) fragments of the amino acid sequence of SEQ ID NO:1, wherein said fragments stimulate growth of avian T lymphocytes expressing γδTCR; or (c) the amino acid sequence of SEQ ID NO:1 having one or more amino acid substitutions, mutations, deletions and insertions and to polynucleotides encoding the amino acid sequences. The present invention further encompasses methods of recombinantly producing said amino acid and polynucleotide sequences and methods of using the amino acid and polynucleotide sequences, particularly for avian vaccines. The sequence of chicken IL-15, SEQ ID Nos:1 and 2 are described. Thus, recombinant fowlpox virus fNZ29R/IL-15 was constructed and purified, and expression of fNZ29R/IL-15 was verified.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 13 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:344861 HCAPLUS
DOCUMENT NUMBER: 131:4240
TITLE: Immunoglobulin molecules having a synthetic variable region and modified specificity
INVENTOR(S): Burch, Ronald M.
PATENT ASSIGNEE(S): Euro-Celtique, S.A., Bermuda
SOURCE: PCT Int. Appl., 123 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9925378	A1	19990527	WO 1998-US24302	19981113
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2309990	AA	19990527	CA 1998-2309990	19981113

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     CA 2310269          AA    19990527    CA 1998-2310269        19981113
     WO 9925379          A1    19990527    WO 1998-US24303        19981113
         W:  AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
             DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE,
             KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW,
             MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR,
             TT, UA, UG, UZ, VN, YU, ZW
         RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
             FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
             CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     AU 9914597          A1    19990607    AU 1999-14597          19981113
     AU 763029           B2    20030710
     AU 9914598          A1    19990607    AU 1999-14598          19981113
     AU 737457           B2    20010823
     EP 1030684          A1    20000830    EP 1998-958584         19981113
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI
     EP 1032420          A1    20000906    EP 1998-958583         19981113
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI
     JP 2001526021       T2    20011218    JP 2000-520811         19981113
     BR 9815289          A     20011226    BR 1998-15289          19981113
     BR 9815580          A     20020129    BR 1998-15580          19981113
     JP 2002507544       T2    20020312    JP 2000-520812         19981113
     ZA 9900048          A     19990708    ZA 1999-48             19990105
     ZA 9900049          A     20000309    ZA 1999-49             19990105
     US 2002028469       A1    20020307    US 2001-963232         20010926
     CA 2461689          AA    20030403    CA 2002-2461689        20020828
     BR 2002012865       A     20040914    BR 2002-12865          20020828
     JP 2005503284       T2    20050203    JP 2003-530495         20020828
     AU 2003252902       A1    20031106    AU 2003-252902         20031010
PRIORITY APPLN. INFO.:                      US 1997-65716P      P  19971114
                                            US 1998-81403P      P  19980410
                                            US 1998-191780      A1 19981113
                                            WO 1998-US24302     W  19981113
                                            WO 1998-US24303     W  19981113
                                            US 2001-963232      A  20010926
                                            WO 2002-US27446     W  20020828
AB   The invention provides modified Ig mols., particularly antibodies, that
     immunospecifically bind a first member of a binding pair which binding
     pair consists of the first member and a second member, which Igs have a
     variable domain containing one or more complimentary determining regions that
     contain the amino acid sequence of a binding site for the second member of
     the binding pair.  The first member is a tumor antigen or an antigen of an
     infectious disease agent, and the second member is a mol. on the surface
     of an immune cell.  The invention further provides for therapeutic and
     diagnostic use of the modified Ig.
REFERENCE COUNT:          13    THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT


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     (FILE 'HOME' ENTERED AT 16:52:27 ON 21 FEB 2006)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 16:52:54 ON 21 FEB 2006
L1          1043 S (ONCOGENEIS OR CANCER OR CELL (A) PROLIFERAT?) AND MYCOPLASMA
L2        115017 S (SIALIC (W) ACID?) OR TRANS-SIALIDASE? OR NEURAMINIDASE?
L3            24 S L1 AND L2
L4            13 DUP REM L3 (11 DUPLICATES REMOVED)

=> e higuchi  m/au
E1            1     HIGUCH T/AU
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E2            7     HIGUCHI/AU
E3            0 --> HIGUCHI  M/AU
E4          825     HIGUCHI A/AU
E5            1     HIGUCHI A E/AU
E6            1     HIGUCHI AIRA/AU
E7            1     HIGUCHI AKI/AU
E8           16     HIGUCHI AKIFUMI/AU
E9           13     HIGUCHI AKIHIKO/AU
E10           3     HIGUCHI AKIHIRA/AU
E11          44     HIGUCHI AKIHIRO/AU
E12          12     HIGUCHI AKIHISA/AU

=> e higuchi  m D L/au
E1            1     HIGUCH T/AU
E2            7     HIGUCHI/AU
E3            0 --> HIGUCHI  M D L/AU
E4          825     HIGUCHI A/AU
E5            1     HIGUCHI A E/AU
E6            1     HIGUCHI AIRA/AU
E7            1     HIGUCHI AKI/AU
E8           16     HIGUCHI AKIFUMI/AU
E9           13     HIGUCHI AKIHIKO/AU
E10           3     HIGUCHI AKIHIRA/AU
E11          44     HIGUCHI AKIHIRO/AU
E12          12     HIGUCHI AKIHISA/AU

=> e schenkman s/au
E1           14     SCHENKMAN ROCILDA P F/AU
E2            1     SCHENKMAN ROCILDA PERAZZINI FUKASAWA/AU
E3          357 --> SCHENKMAN S/AU
E4            4     SCHENKMAN S */AU
E5            1     SCHENKMAN S P/AU
E6            5     SCHENKMAN S S/AU
E7            2     SCHENKMAN SELVA S/AU
E8          120     SCHENKMAN SERGIO/AU
E9            2     SCHENKMAN SIMONE/AU
E10           1     SCHENKMANM RONNI L/AU
E11           2     SCHENKMANN A/AU
E12           3     SCHENKMANN N S/AU

=> s e3
L5          357 "SCHENKMAN S"/AU

=> s e3-e8
L6          489 ("SCHENKMAN S"/AU OR "SCHENKMAN S *"/AU OR "SCHENKMAN S P"/AU
                OR "SCHENKMAN S S"/AU OR "SCHENKMAN SELVA S"/AU OR "SCHENKMAN
                SERGIO"/AU)

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     (FILE 'HOME' ENTERED AT 16:52:27 ON 21 FEB 2006)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 16:52:54 ON 21 FEB 2006
L1          1043 S (ONCOGENEIS OR CANCER OR CELL (A) PROLIFERAT?) AND MYCOPLASMA
L2        115017 S (SIALIC (W) ACID?) OR TRANS-SIALIDASE? OR NEURAMINIDASE?
L3            24 S L1 AND L2
L4            13 DUP REM L3 (11 DUPLICATES REMOVED)
                 E HIGUCHI  M/AU
                 E HIGUCHI  M D L/AU
                 E SCHENKMAN S/AU
L5           357 S E3
L6           489 S E3-E8
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=> s l2 and l6
L7          241 L2 AND L6

=> s l1 and l7
L8            3 L1 AND L7

=> dup rem l8
PROCESSING COMPLETED FOR L8
L9            3 DUP REM L8 (0 DUPLICATES REMOVED)

=> d 1-3 ibib ab

L9    ANSWER 1 OF 3  BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2004-00309  BIOTECHDS
TITLE:            Use of an agent that prevents or inhibits Mycoplasma
                  infection, for manufacturing a medicament for treating or
                  preventing a disorder associated with increased cell
                  proliferation, e.g. atherosclerotic vascular disease
                  or malignancy;
                     recombinant Trypanosoma cruzi protein application in
                     infection, tumor and vascular disease therapy
AUTHOR:           HIGUCHI M D L; SCHENKMAN S
PATENT ASSIGNEE:  HIGUCHI M D L; SCHENKMAN S
PATENT INFO:      US 2003124109 3 Jul 2003
APPLICATION INFO: US 2002-86913 1 Mar 2002
PRIORITY INFO:    BR 2001-2648 3 Jul 2001; BR 2000-2989 3 Jul 2000
DOCUMENT TYPE:    Patent
LANGUAGE:         English
OTHER SOURCE:     WPI: 2003-810968 [76]
AB    DERWENT ABSTRACT:
      NOVELTY - Use of an agent that prevents or inhibits Mycoplasma
      infection for manufacturing a medicament for treating a disorder
      associated with increased cell proliferation.
           DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for a
      composition for treating or preventing Mycoplasma infection in
      a subject suffering from a disorder associated with increased
      cell proliferation or a co-infection with
      mycoplasma and a second microbe, comprising an agent that
      prevents or inhibits sialic acid-mediated attachment
      of mycoplasma to cells of the subject.
           BIOTECHNOLOGY - Preferred Composition: The agent is an antibiotic or
      an enzyme having an activity consisting of neuraminidase and/or
      trans-sialidase activity. The enzyme is derived from a
      Trypanosoma cruzi microorganism, where the enzyme is a native or a
      recombinant enzyme. The enzyme has a fully defined sequence of 669 amino
      acids given in the specification. A vector containing the DNA insert
      having a fully defined sequence of 2010 bp given in the specification
      produces the enzyme.
           ACTIVITY - Antibacterial; Antiarteriosclerotic; Cytostatic;
      Anti-HIV. A 64-year-old female patient with a palpable abdominal mass and
      a tumoral mass in the rectum was administered 50 ml of native
      trans-sialidase (TSN) intraperitoneally on alternate
      days for a period of 14 days. On day 23, with mycoplasmas
      confirmed in the bone marrow, erythromycin (500 mg/day) was given for a
      further 20 days. Clinical improvement and normalization of blood
      leukocytes was seen after 2 days. Considering the important clinical
      improvement and reduction in abdominal mass, a second session of TSN was
      administered. The patient demonstrated improvement in general clinical
      status. Tomography detected a reduction in tumoral mass. Results showed
      that trans-sialidase is effective as a drug in the
      treatment of neoplasia, removing mycoplasmas from the
      neoplastic cells leading to their apoptosis.
           MECHANISM OF ACTION - Neuraminidase; Trans-
      sialidase.
```

USE - The composition or the agent that prevents or inhibits **mycoplasma** infection is useful for manufacturing a medicament for treating or preventing a disorder associated with increased **cell proliferation**, e.g. atherosclerotic vascular disease or malignant disease, or a disease associated with co-infection with **mycoplasma** and a second microbe such as human immunodeficiency virus or a Chlamydia microbe (all claimed).

ADMINISTRATION - The amount of the enzyme administered is about 106-1013 units per day. Administration may be intravenous, intraperitoneal, intrathecal, oral, by inhalation, subcutaneous, or intramuscular. (32 pages)

L9 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:654898 HCAPLUS
DOCUMENT NUMBER: 143:126750
TITLE: Prevention and treatment of diseases associated with **Mycoplasma**
INVENTOR(S): Higuchi, Maria de Lourdes; **Schenkman, Sergio**
PATENT ASSIGNEE(S): Brazil
SOURCE: Braz. Pedido PI, 65 pp.
CODEN: BPXXDX
DOCUMENT TYPE: Patent
LANGUAGE: Portuguese
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
BR 2001002648	A	20030708	BR 2001-2648		20010703
CA 2383850	AA	20020110	CA 2001-2383850		20010703
US 2003124109	A1	20030703	US 2002-86913		20020301
US 2005142116	A1	20050630	US 2004-952003		20040928
PRIORITY APPLN. INFO.:			BR 2000-2989	A	20000703
			BR 2001-2648	A	20010703
			WO 2001-BR83	W	20010703
			US 2002-86913	A2	20020301
			BR 2002-1010	A	20020328
			WO 2003-BR49	A2	20030328

AB The invention pertains to treatment of diseases associated with undesirable cellular proliferation, including arteriosclerotic narrowing of blood vessels, by preventing infection by **mycoplasmas**. This is based upon the discovery that **Mycoplasma** is involved in many cases of undesirable cellular proliferation.

L9 ANSWER 3 OF 3 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2002-08674 BIOTECHDS
TITLE: Composition useful for treatment of **mycoplasma** infection and diseases associated with **cell proliferation** e.g. malignancy or with co-infection with another microbe, comprises agent inhibiting **sialic acid**-mediated attachment of **mycoplasma**;
native or recombinant enzyme treatment and vector-mediated gene transfer and expression in host cell for disease therapy or prevention
AUTHOR: HIGUCHI M D L; **SCHENKMAN S**
PATENT ASSIGNEE: HIGUCHI M D L; SCHENKMAN S
PATENT INFO: WO 2002002050 10 Jan 2002
APPLICATION INFO: WO 2000-BR83 3 Jul 2000
PRIORITY INFO: BR 2000-2989 3 Jul 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-154675 [20]
AB DERWENT ABSTRACT:

NOVELTY - A composition useful for treating or preventing **mycoplasma** infection in a subject suffering from a disorder characterized by increased **cell proliferation** or by co-infection with a second microbe comprising an agent that prevents or inhibits **sialic acid**-mediated attachment of **mycoplasma** to the subject's cells, is new.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for use of an agent preventing/inhibiting **mycoplasma** infection in medicaments to treat disorders characterized by increase **cell proliferation**.

BIOTECHNOLOGY - Preferred Composition: The agent is preferably an enzyme (native or recombinant) with **neuraminidase** and/or **trans-sialidase** activity, especially derived from Trypanosoma cruzi. It preferably has fully defined sequence (I) of 669 amino acids as given in the specification. The medicament preferably includes a vector comprising DNA insert of a fully defined sequence (II) of 2010 base pairs as given in the specification, producing the preferred enzyme having sequence (I) as above.

ACTIVITY - Antiatherosclerotic; antibacterial; antiviral; anti-HIV; cytostatic; vasotropic. A laboratory rat population was determined to be infected with both **Mycoplasma** pulmonis and Chlamydia pneumoniae using standard immunohistological techniques and histological examination of various organs. Nine adult rats (approximately 285 g; seven males, two females) presenting conjunctivitis, slow movements and, in one rat severe otitis and another severe weight loss, were allocated to groups A or B. A (Control group) comprised three animals, two of which were killed without injecting any substance and one receiving an inactivated form of 'TSC' (recombinantly produced catalytic portion of Trypanosoma cruzi **trans-sialidase**) for 5 consecutive days. B comprised five animals receiving 'TNS' (complete, native Trypanosoma cruzi **trans-sialidase**) (0.5 ml/animal, every 2 days) and sacrificed after 7, 9, and 12 days, and one rat receiving active TSC (140 microgram/day, five consecutive days) and killed after 7 days. Group B rats showed a clear improvement in symptoms, becoming more agile, requiring more ether to anesthetize them and becoming more difficult to restrain. The animal with otitis showed less equilibrium loss and the animal with severe weight loss gained weight. Since the lung was the most frequently injured organ, pulmonary alterations were examined using electron microscopy, confocal laser microscopy and immunohistochemistry. Histological sections showed that treated animals presented resolving pneumonitis after 7 d. After 9-12 days M. pulmonis were almost absent from alveoli and mean C. pneumoniae positive cell numbers in alveoli had decreased, compatible with regression of C. pneumoniae infection. Results are given in the specification.

MECHANISM OF ACTION - Inhibits **sialic acid** mediated attachment of **mycoplasma** to cells.

USE - The compositions are useful to treat diseases associated with undesirable **cell proliferation**, such as atherosclerotic vascular disease and malignancy (both claimed), by reducing or preventing **mycoplasma** infection. They also useful to treat diseases associated with infection with other infectious organisms co-occurring with **mycoplasma** (and typically increasing the virulence of both pathogens), especially human immunodeficiency virus or chlamydia species. They can be used to treat such diseases in humans or other animals, and can be administered in conjunction with conventional agents e.g. anti-platelet or chemotherapeutic agents.(63 pages)

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FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,

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                 E HIGUCHI  M D L/AU
                 E SCHENKMAN S/AU
L5           357 S E3
L6           489 S E3-E8
L7           241 S L2 AND L6
L8             3 S L1 AND L7
L9             3 DUP REM L8 (0 DUPLICATES REMOVED)
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